

# Decoding the epigenome to navigate human health

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E P I N  M I C S

# Epigenome is the instructions for using genome hardware

## Hardware



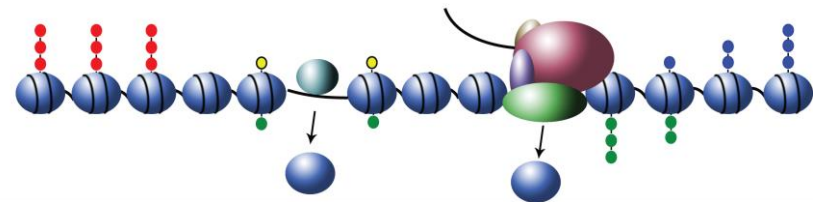
## Software



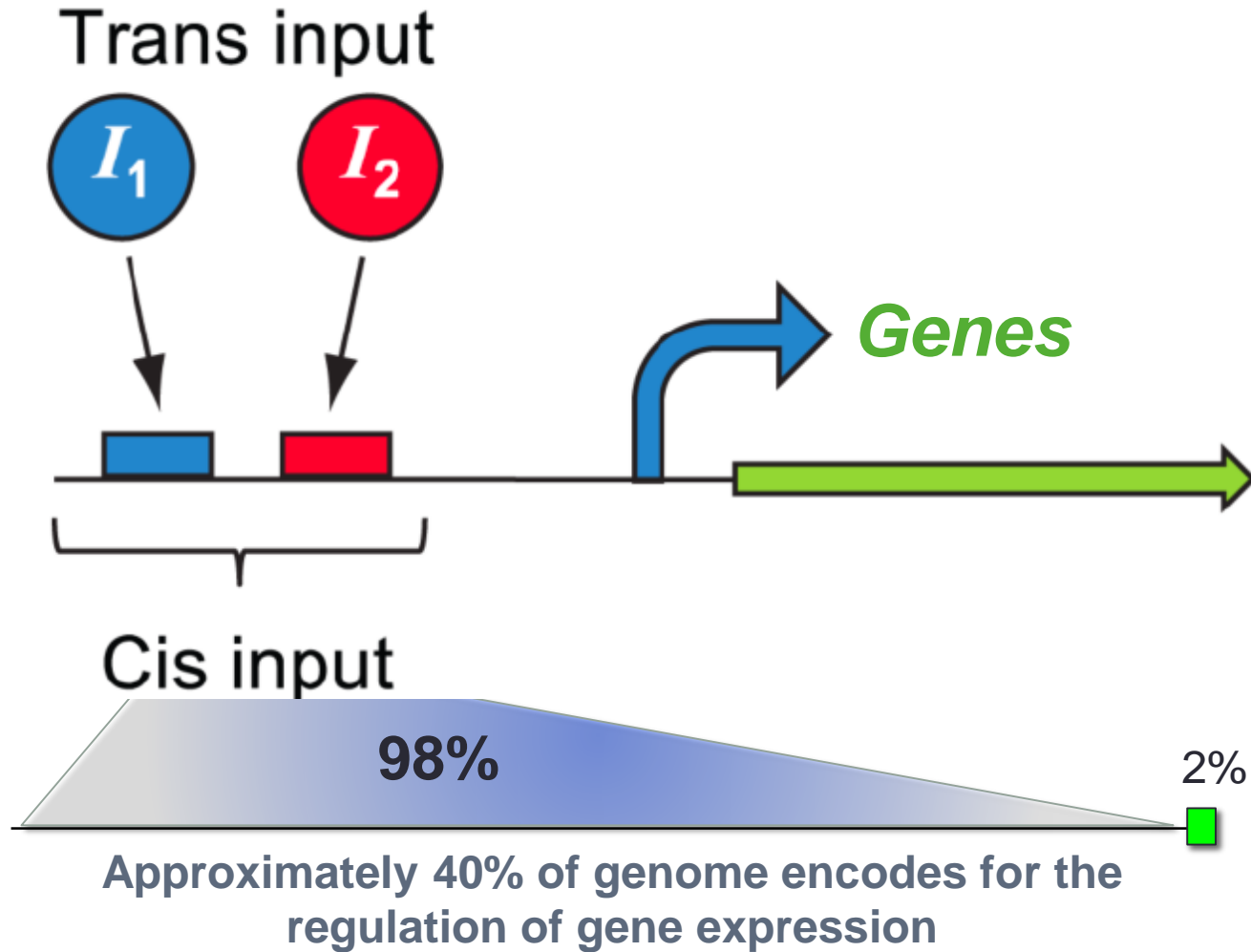
## Genome



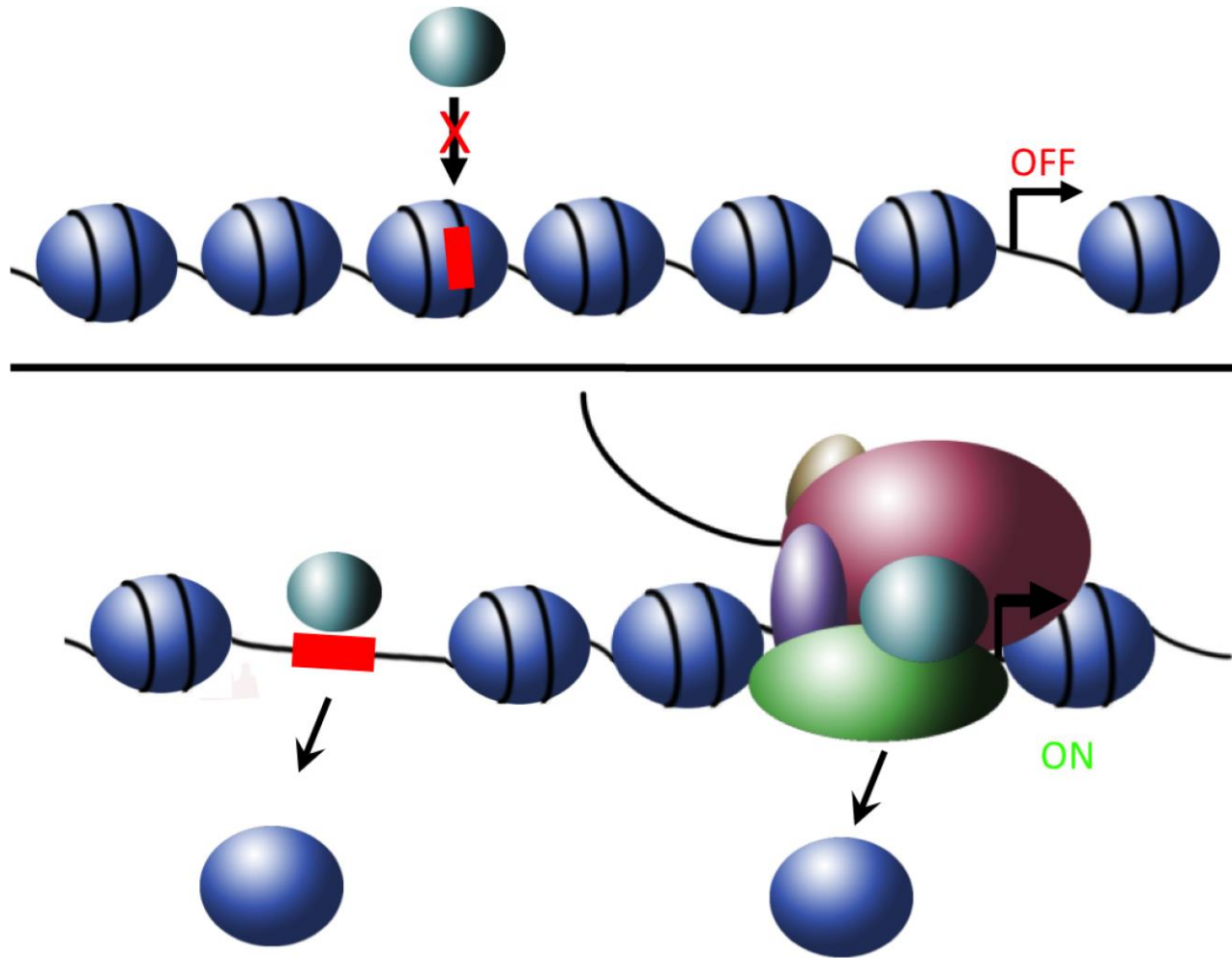
## Epigenome



# Instructions encoded within non-coding sequence



# Access to regulatory information controlled by epigenome



Nucleosome



DNA binding motif

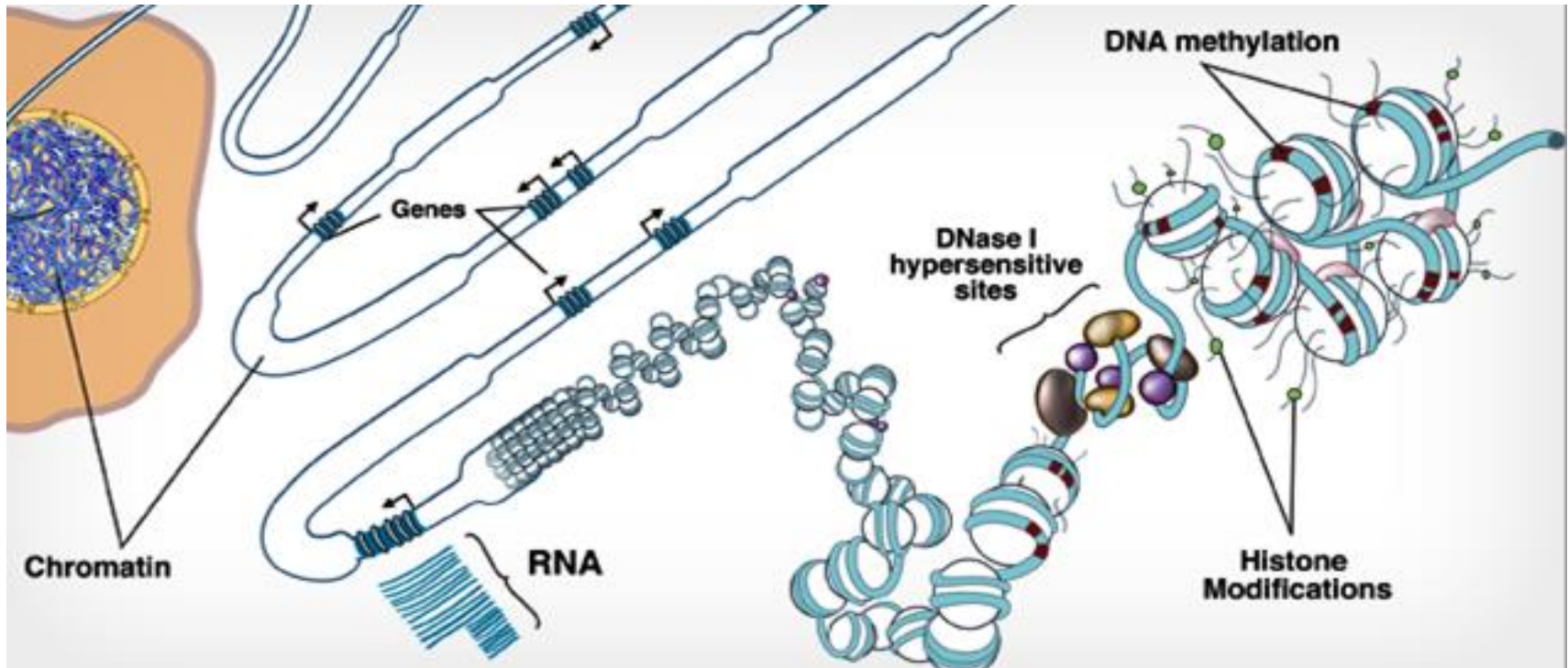


DNA binding protein



RNA Polymerase

# Techniques for measuring epigenomic features



Output

Direct measures

RNA

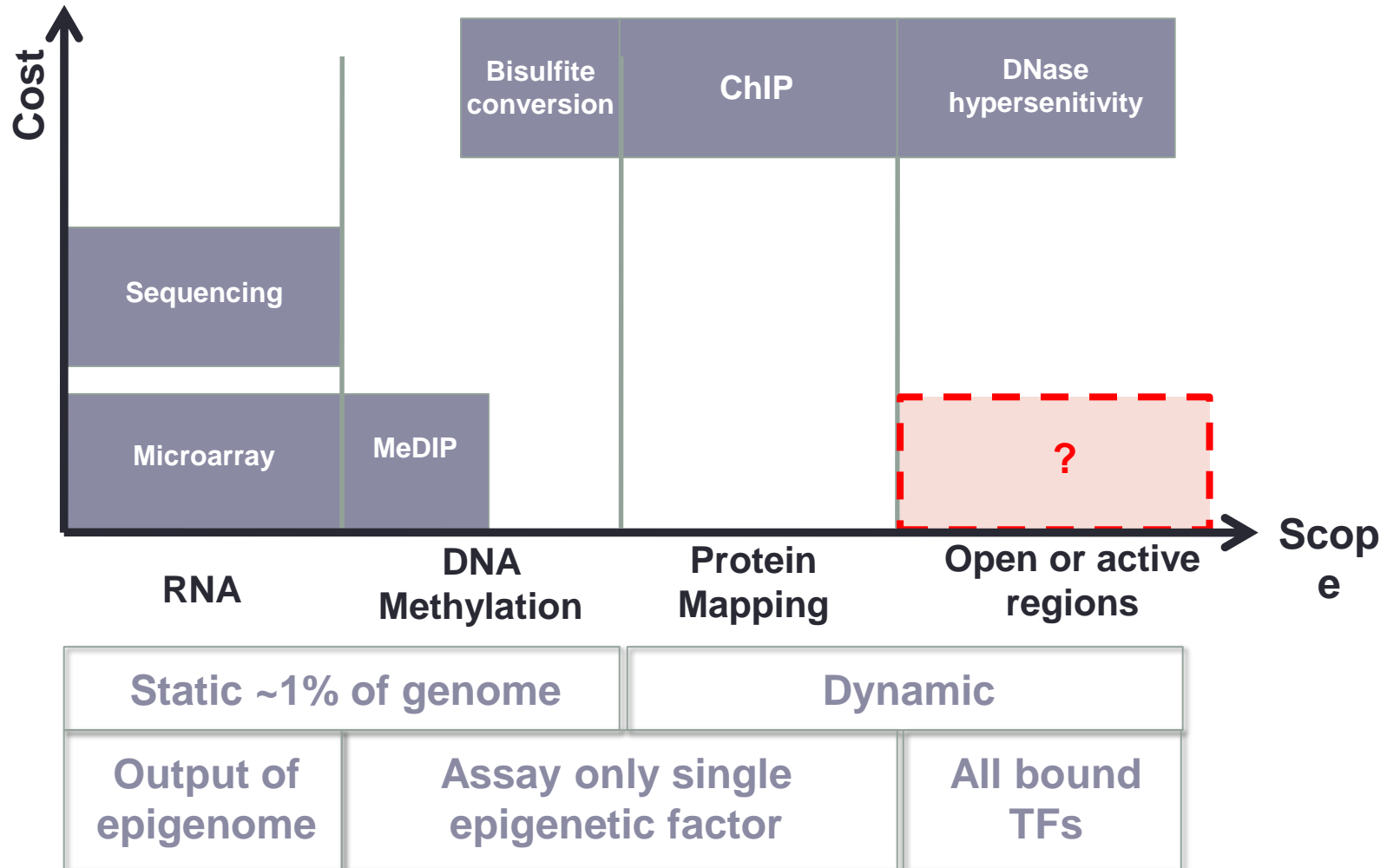
DNA  
Methylation

Protein-DNA  
Mapping

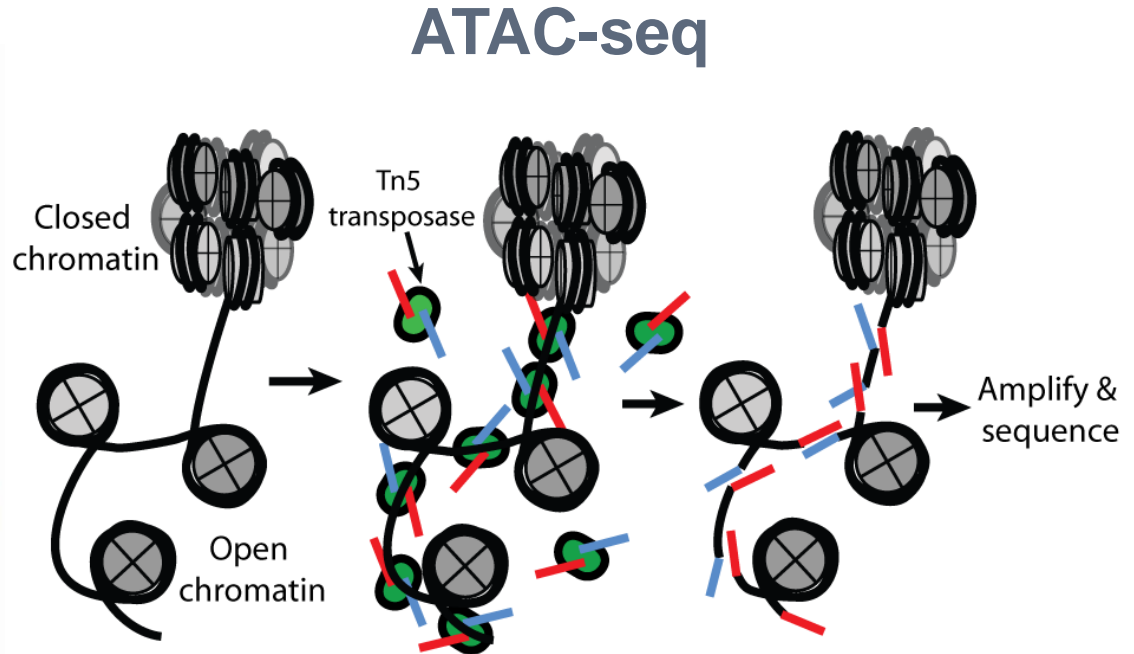
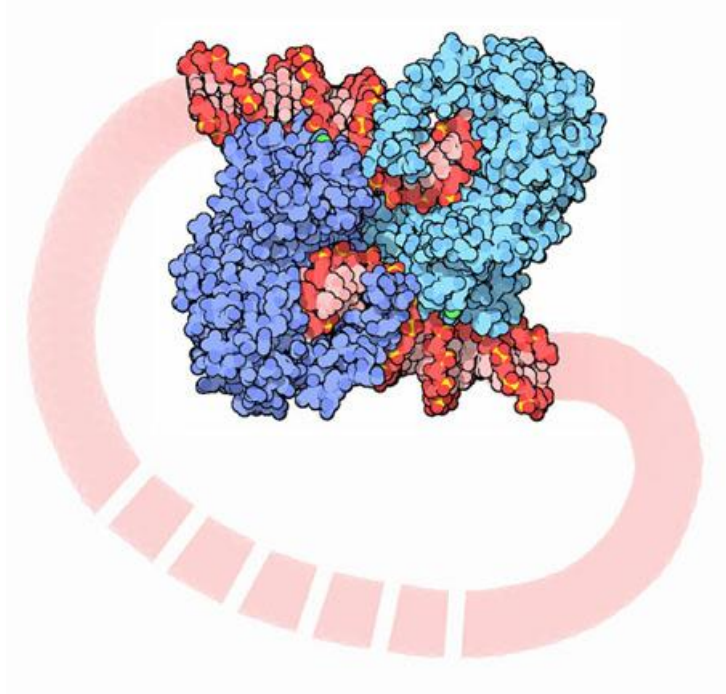
Accessibility

# Landscape of technologies for measuring epigenome

## TECHNOLOGY LANDSCAPE



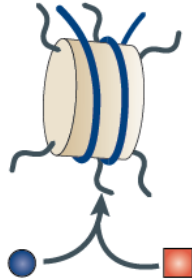
# Rapid and efficient technology for profiling the epigenome





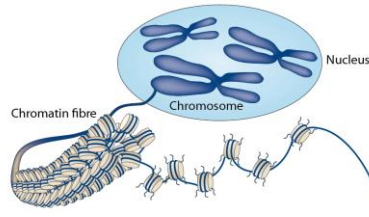
# Rapid and efficient technology for profiling the epigenome

## ChIP-seq



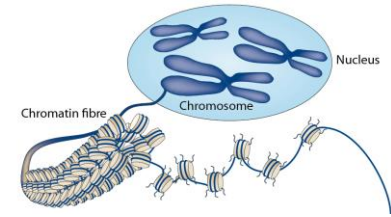
$10^7$  cells

## DNase-seq



$10^7$  cells

## ATAC-seq



100-50,000 cells

Input  
requirement

Sample prep  
time

Outputs

- Measures single factor only
- Limited factors can be probed

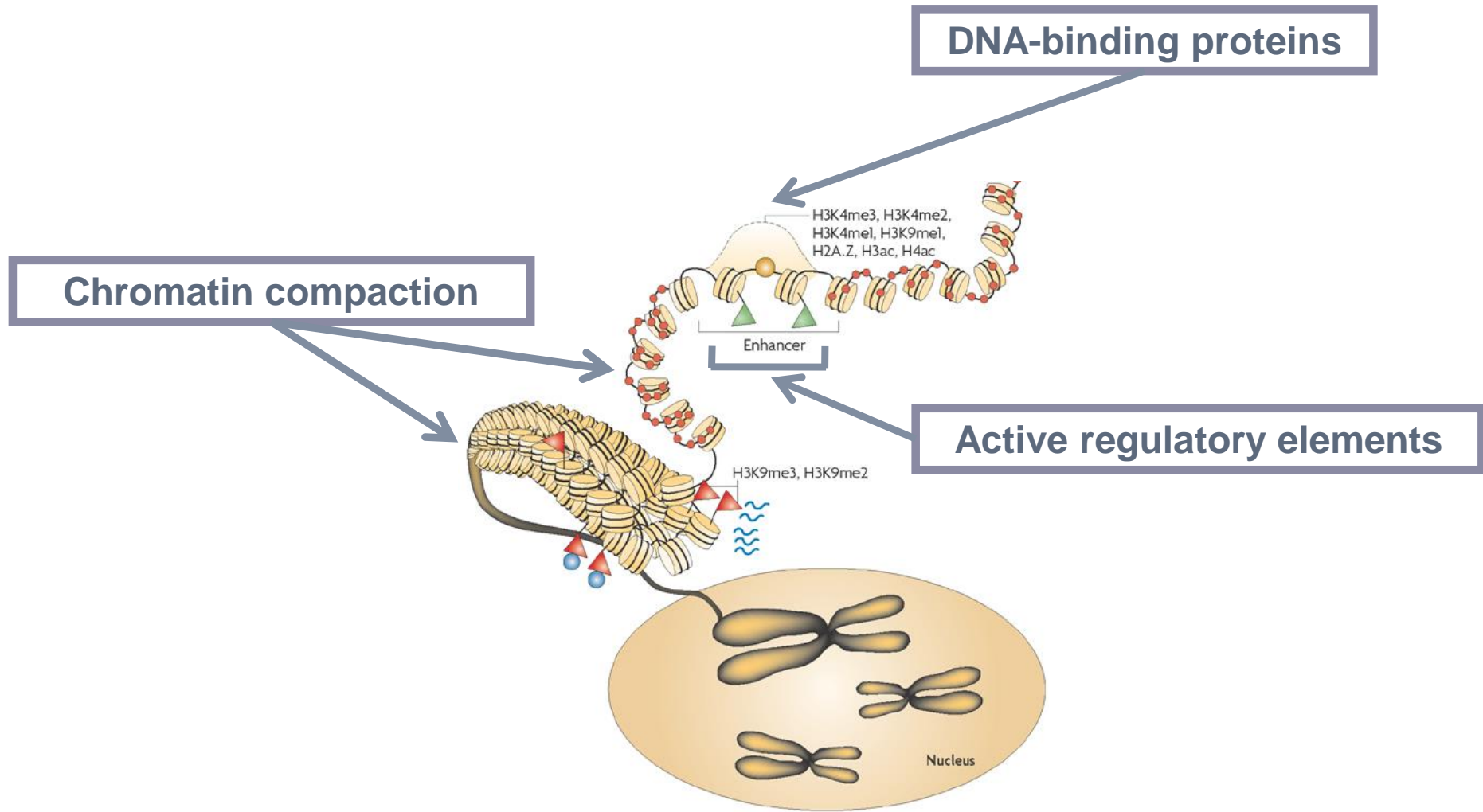
- High skills required to reproduce

- All proteins bound to genome in 1 reaction
- Higher-order chromatin compaction

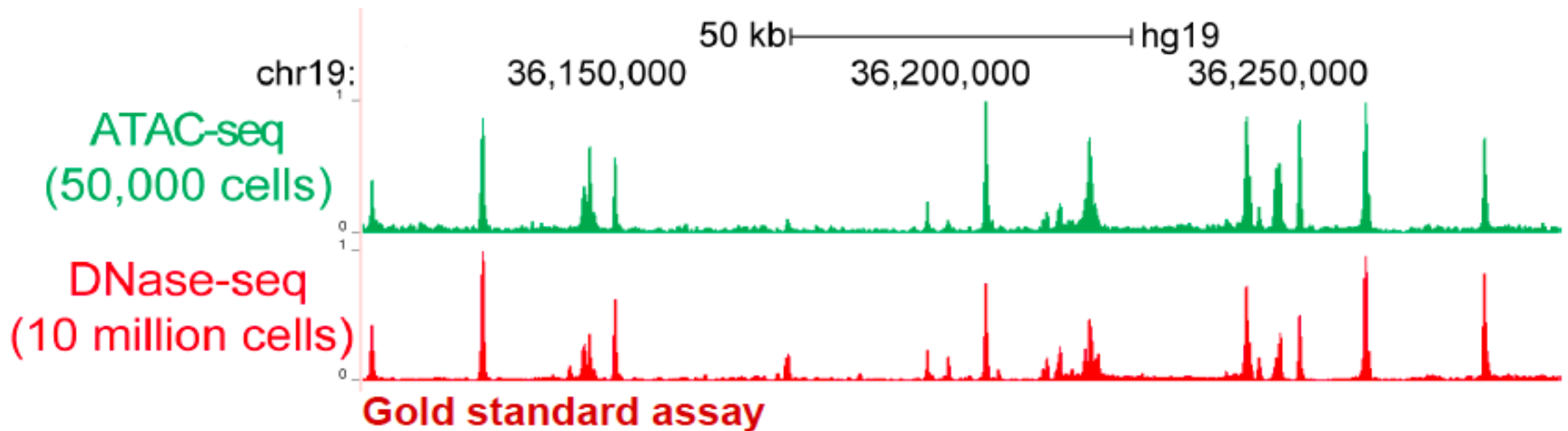
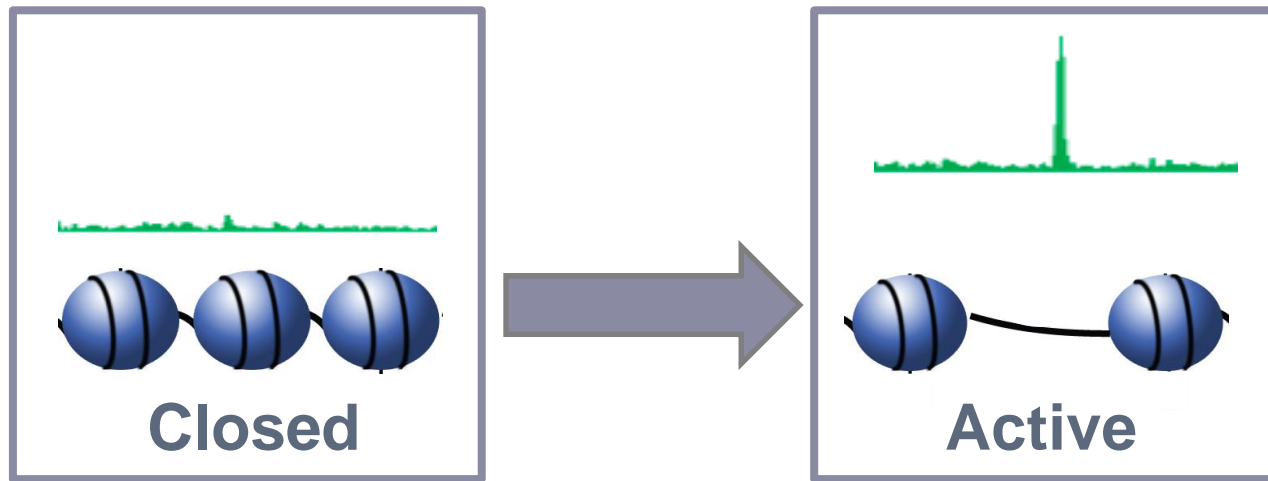




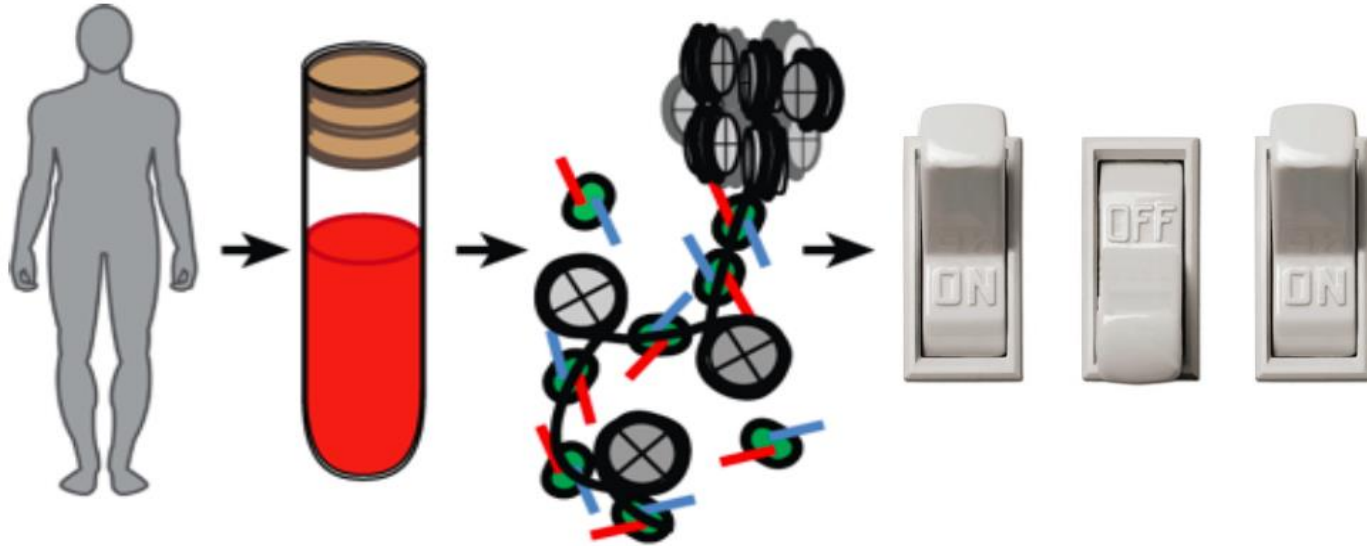
# Types of epigenomic features measured using ATAC-seq



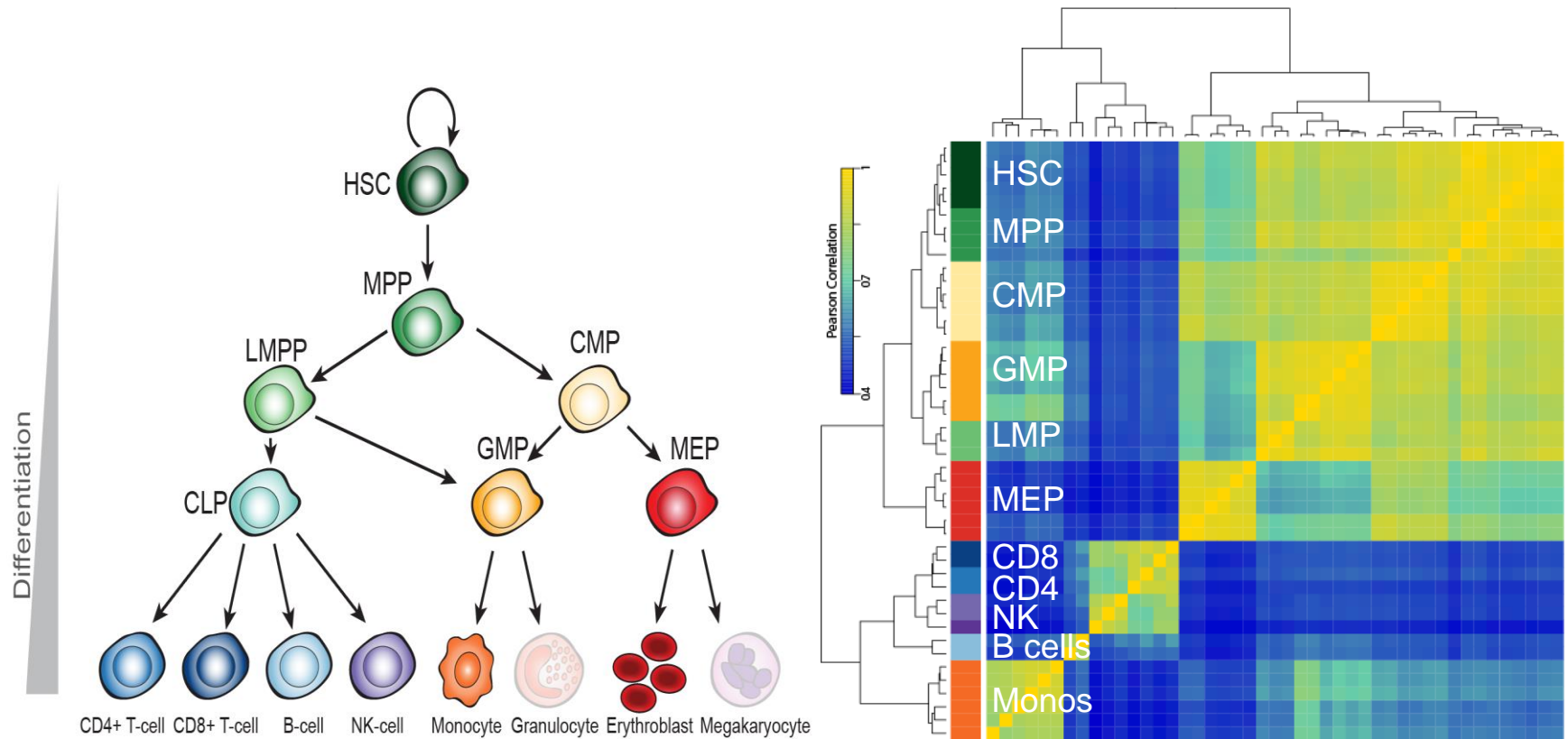
# Identification of active regulatory elements from limited number of cells



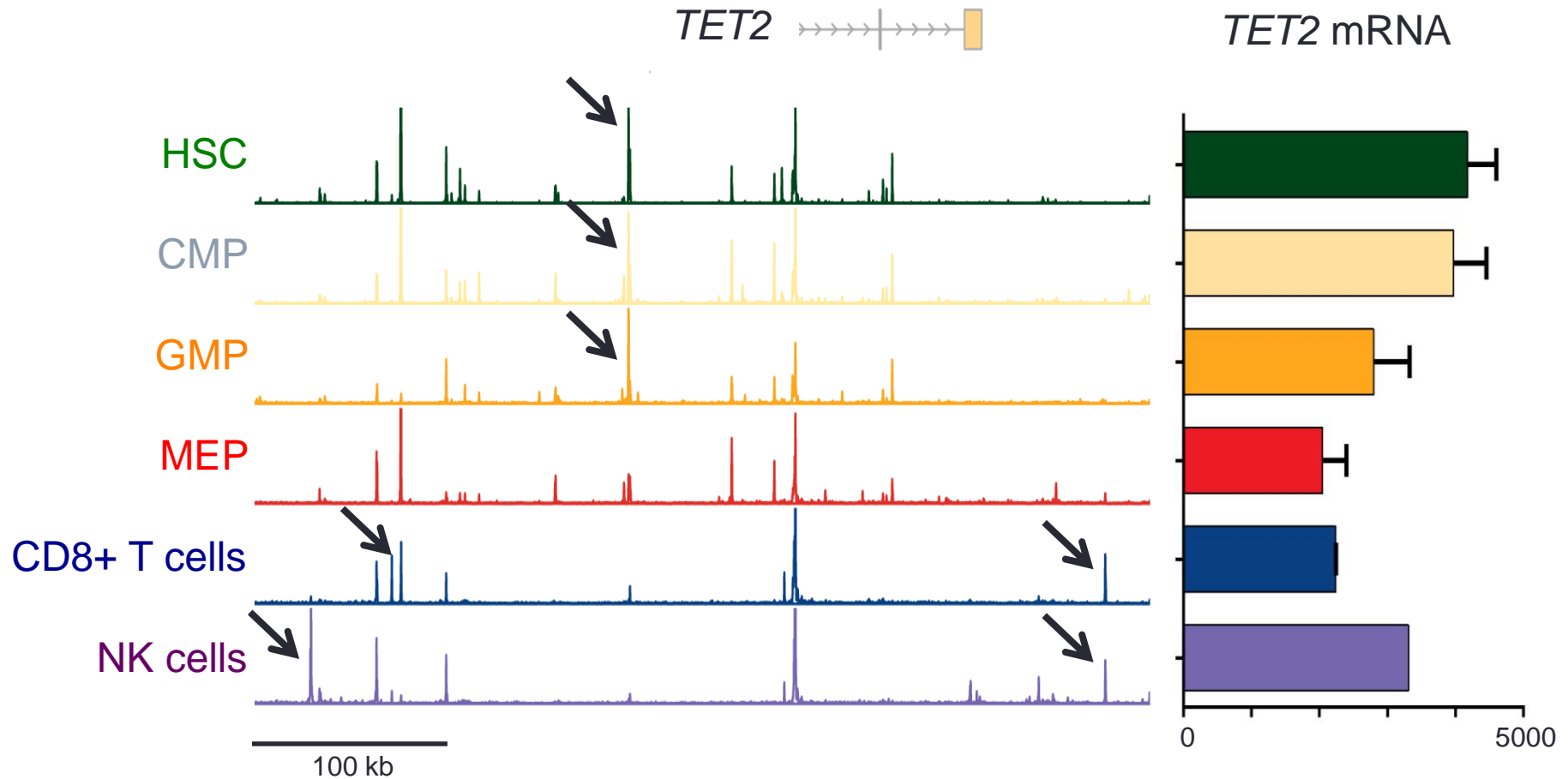
# Compatible with fresh and archived blood samples



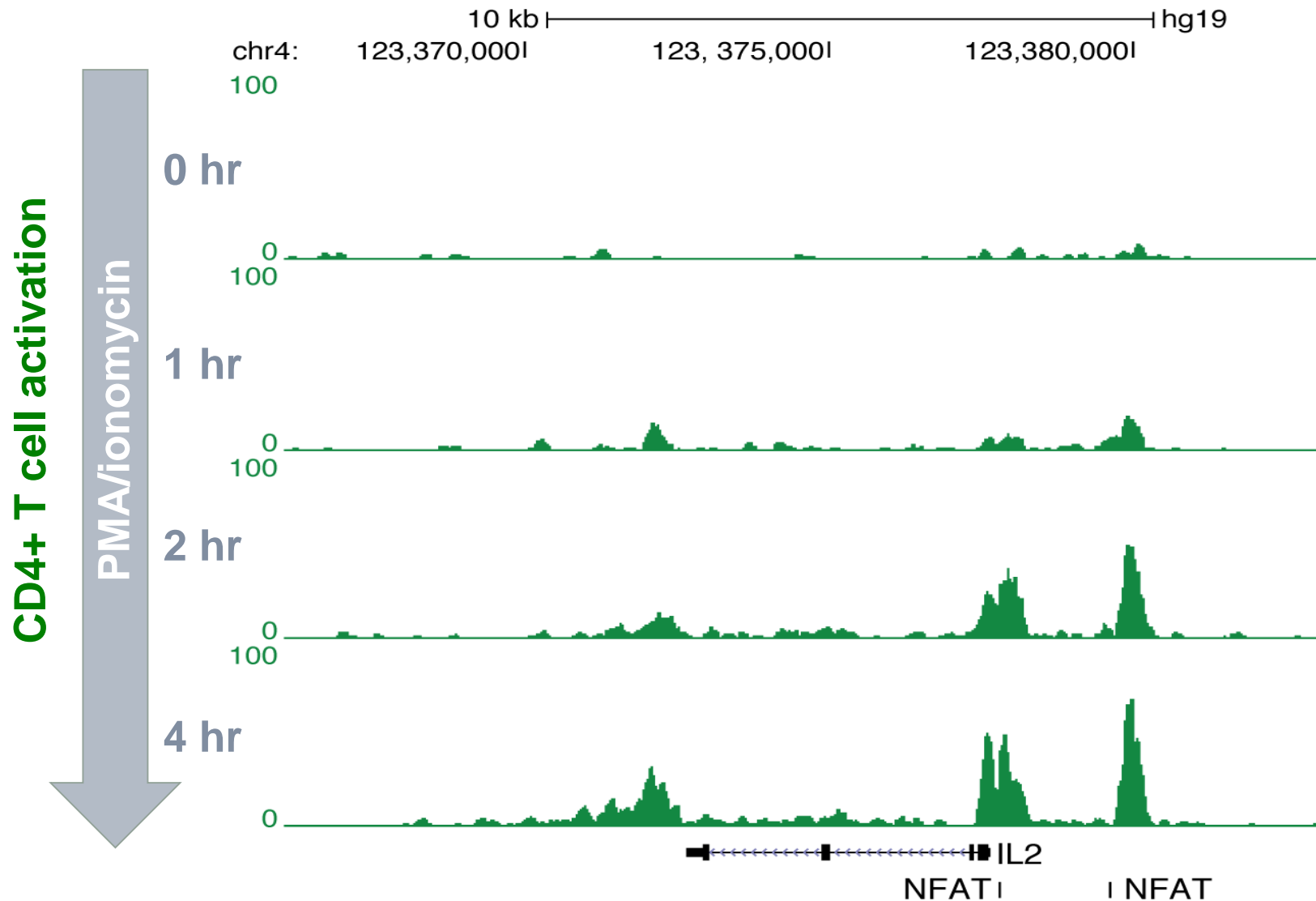
# Landscape of hematopoietic development



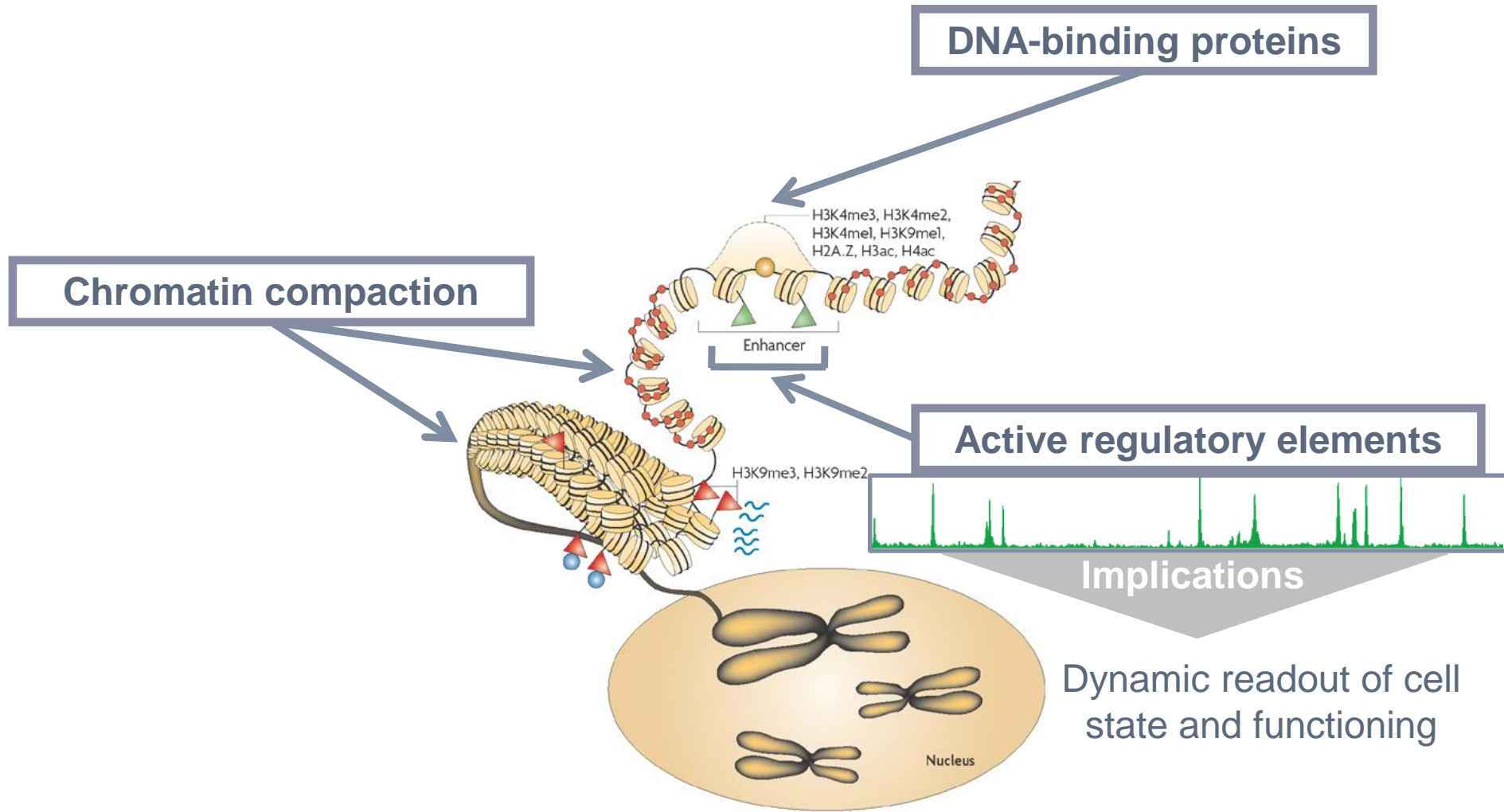
# Active regulatory elements are fingerprint of cell identity



# Rapid and sensitive detection of epigenomic modulation

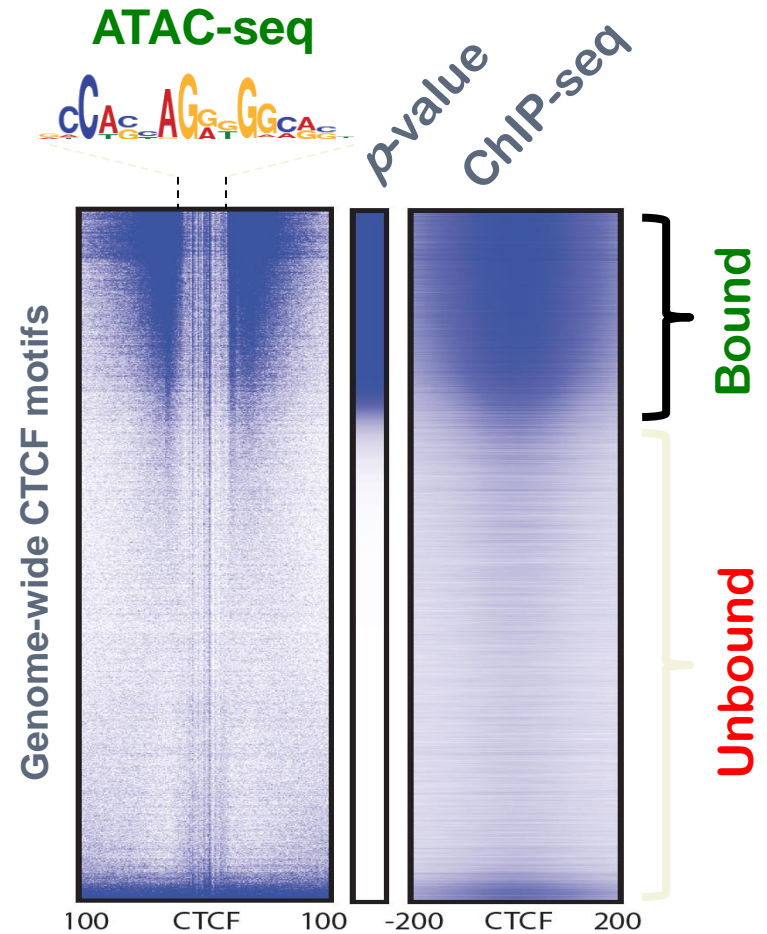
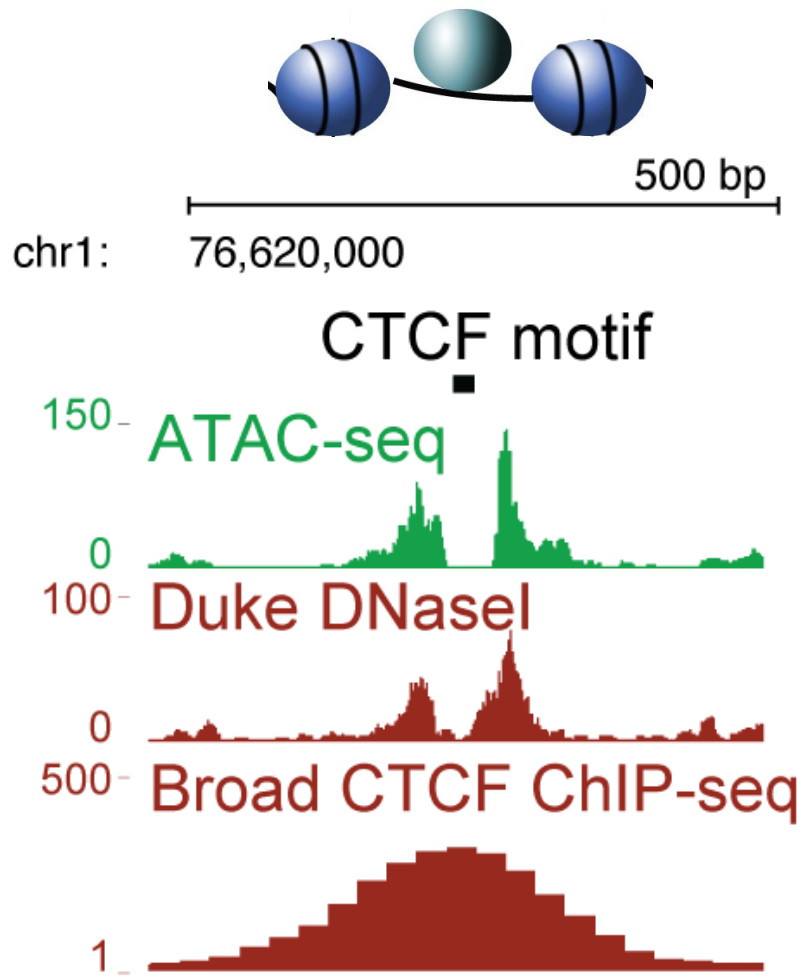


# Rapid and efficient technology for profiling the epigenome



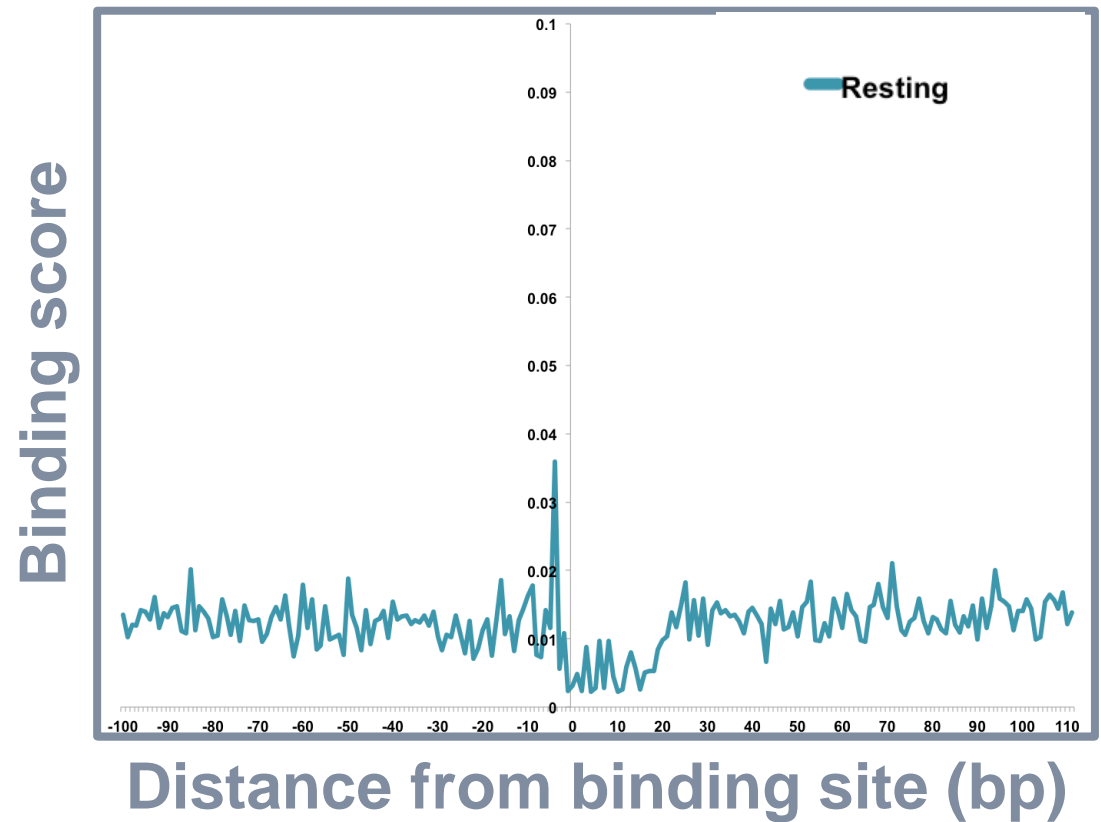


# Binding locations of hundreds of factors read out at once

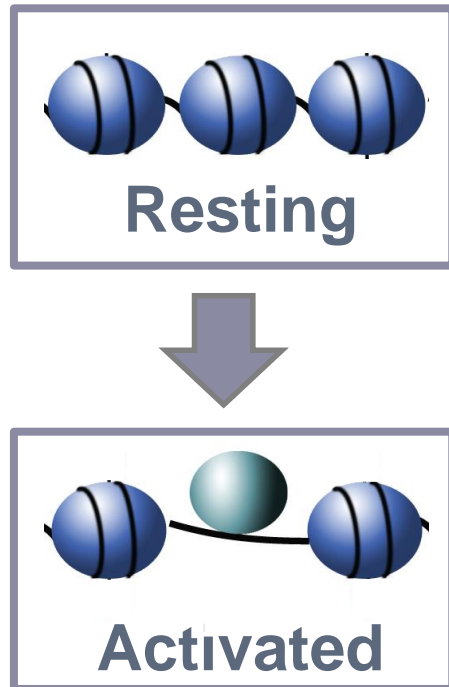


# Detection of therapeutic modulation of epigenomic factors

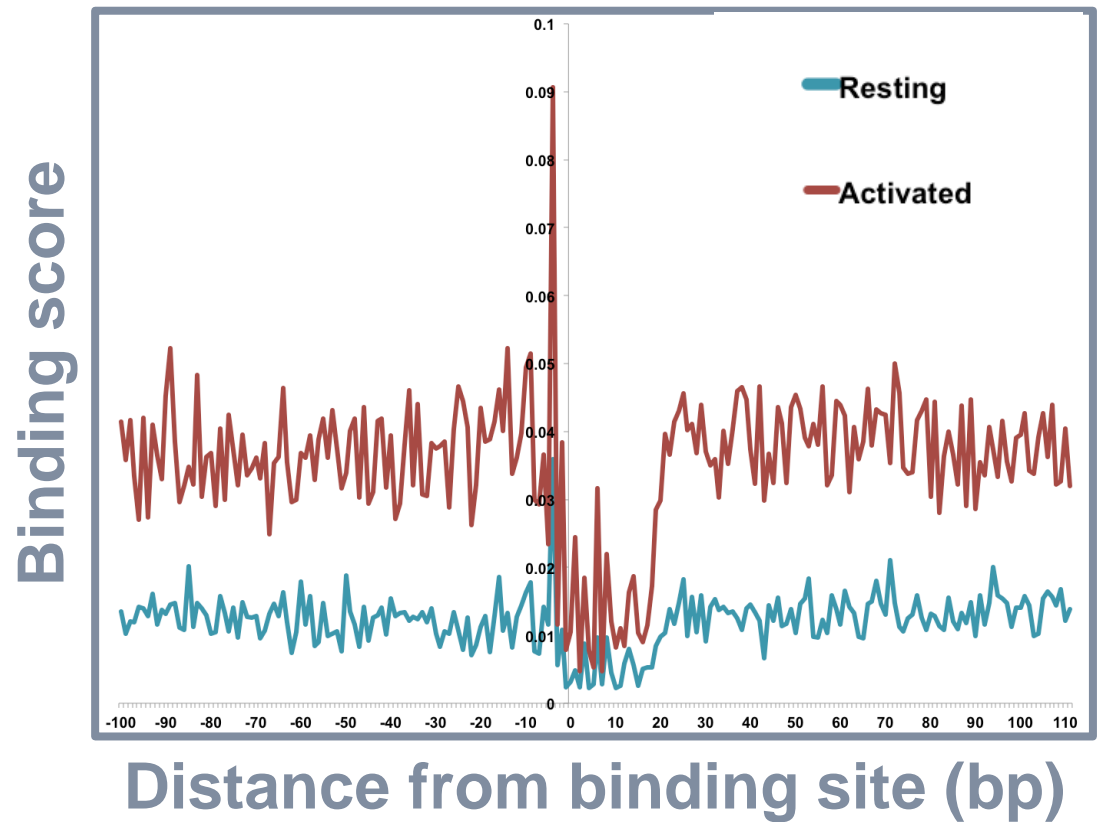
## CD4+ T cell activation NFAT



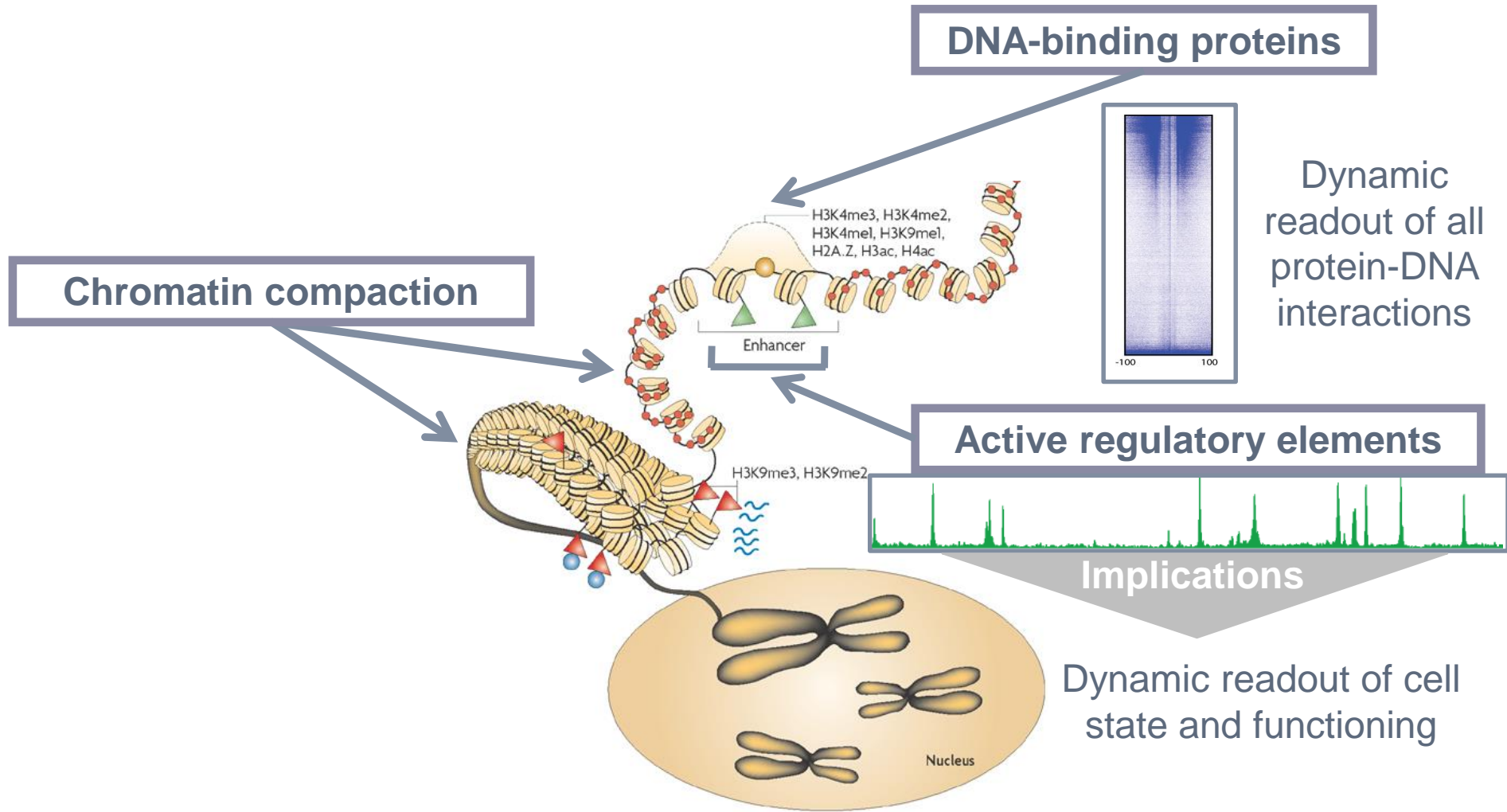
# Detection of therapeutic modulation of epigenomic factors



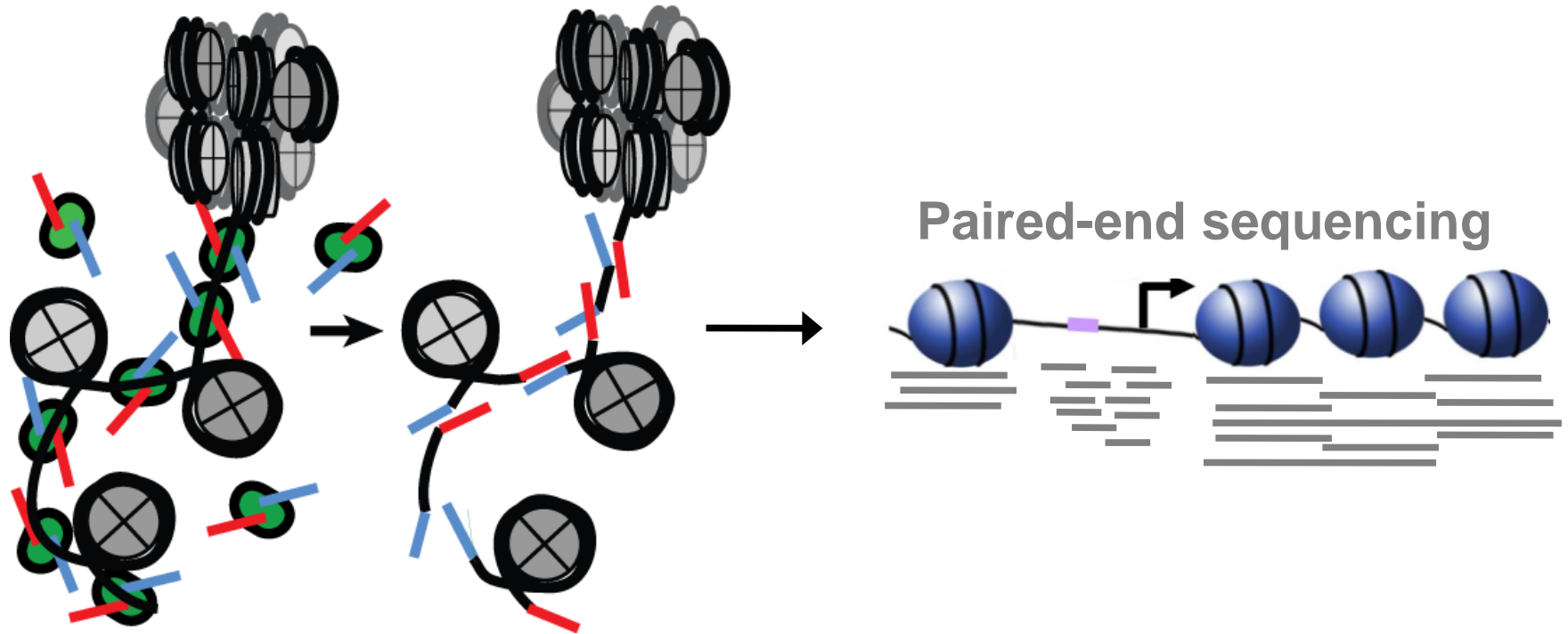
## CD4+ T cell activation NFAT



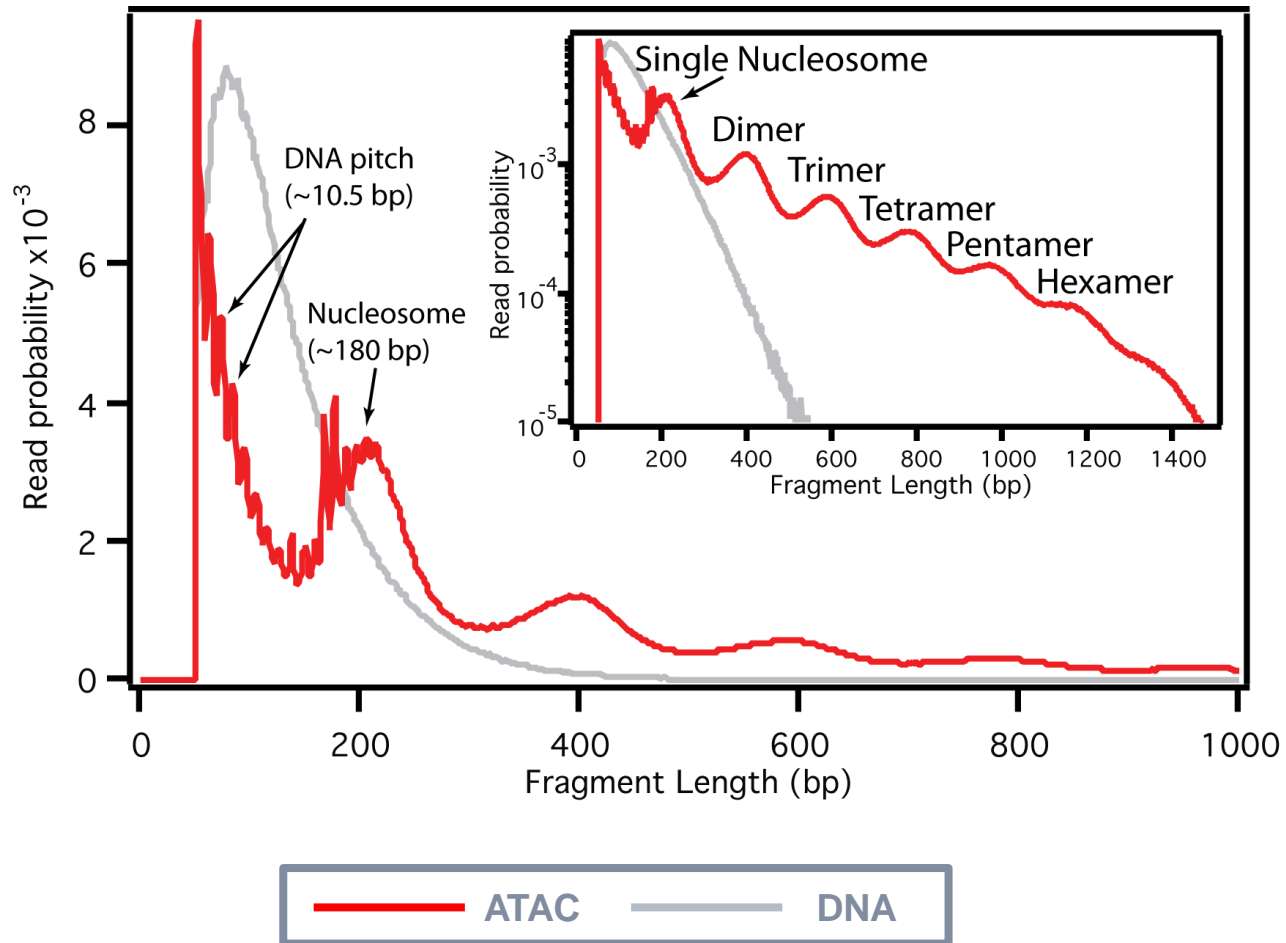
# Rapid and efficient technology for profiling the epigenome



# Distribution of fragment lengths driven by chromatin

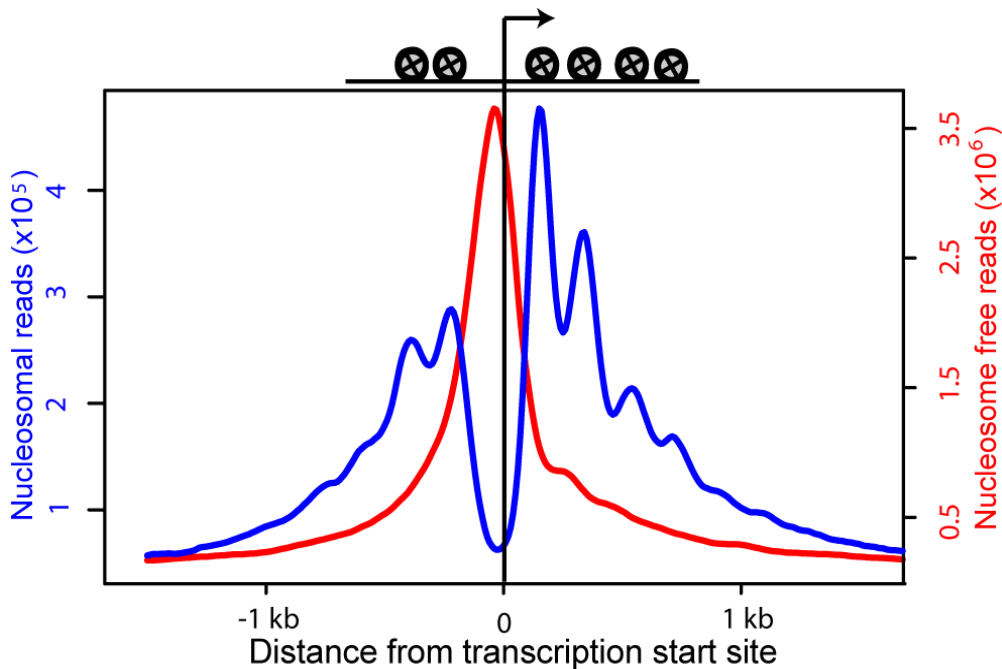


# Distribution of fragment lengths driven by chromatin

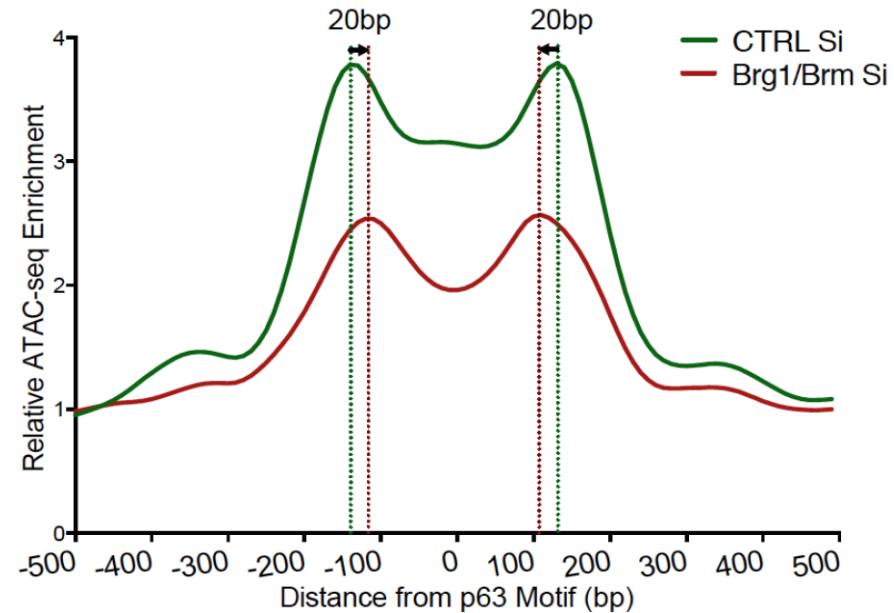


# Single basepair resolution nucleosome positioning

## Detection of nucleosome organization at transcription start sites

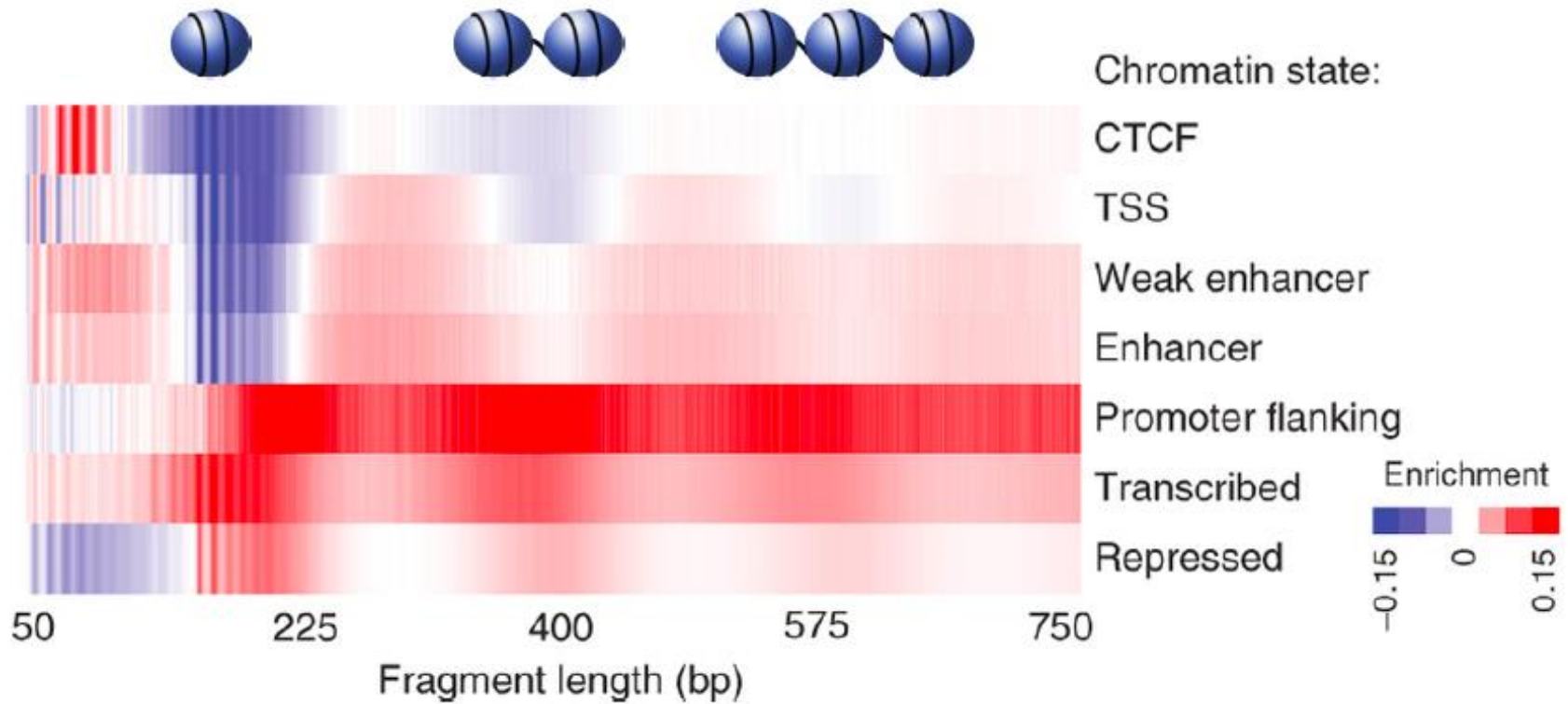


## Detection of nucleosome positioning with loss of chromatin remodeling complex



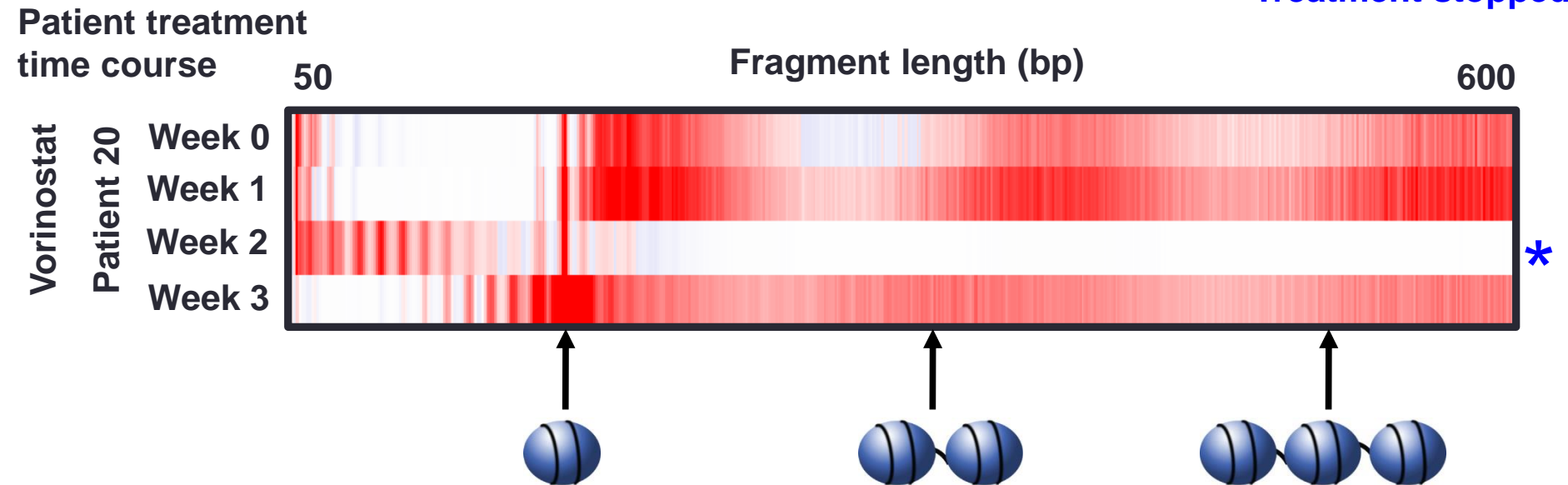


# Determination of functional epigenomic states

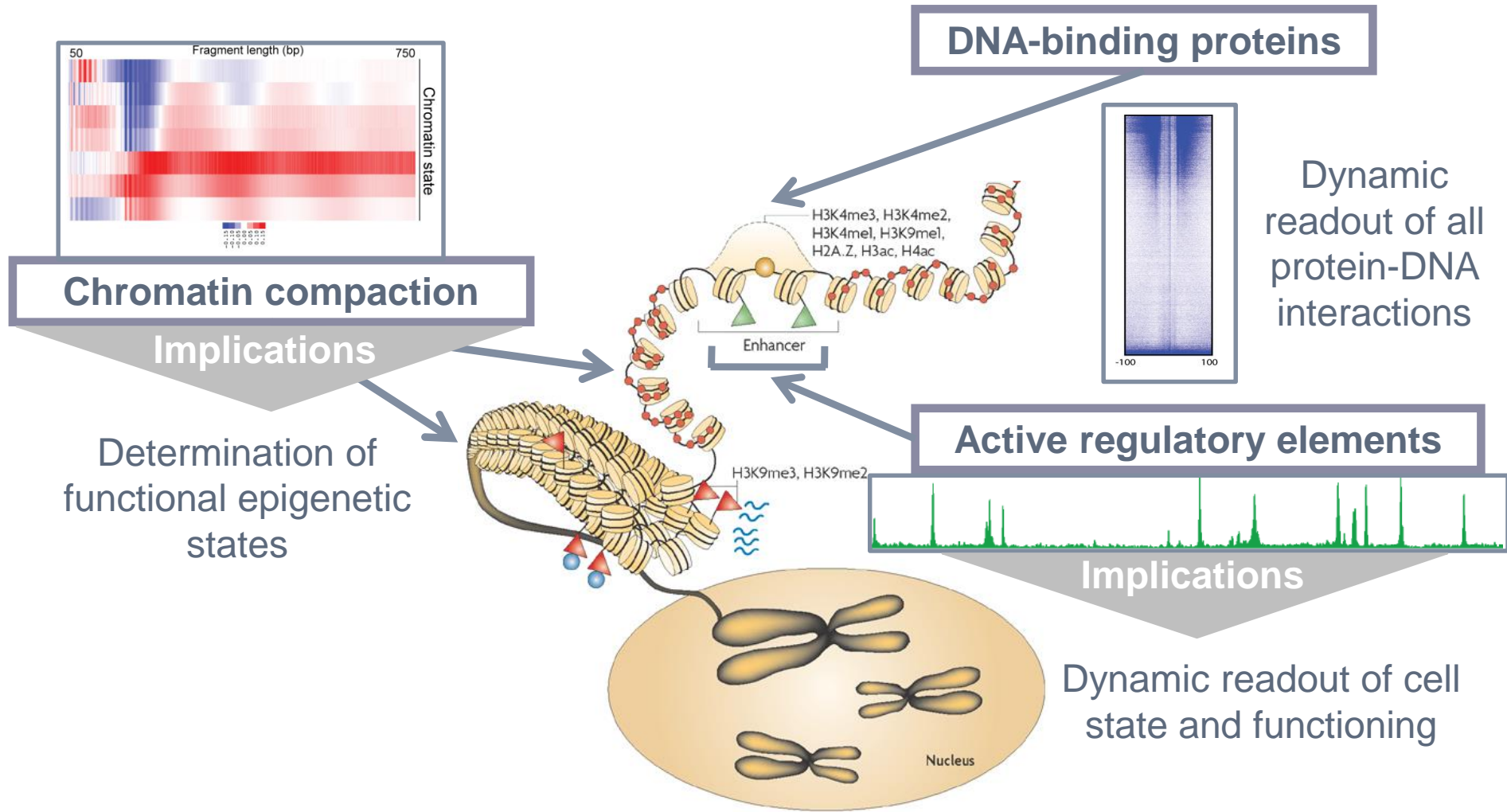


# Real time monitoring of epigenomic changes in patients

\* Treatment stopped

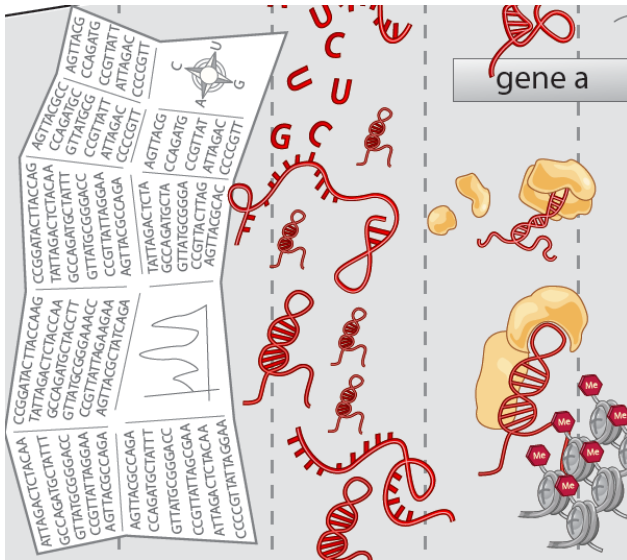


# Rapid and efficient technology for profiling the epigenome



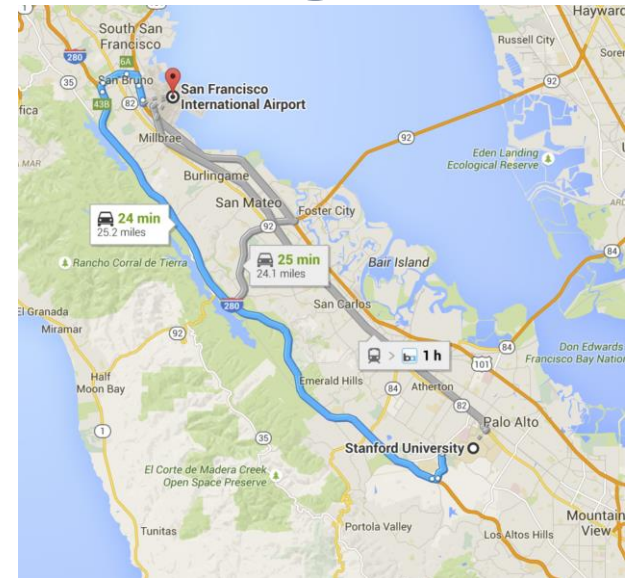
# Mapping epigenomic landscape to create purposeful navigation

## Reference Maps



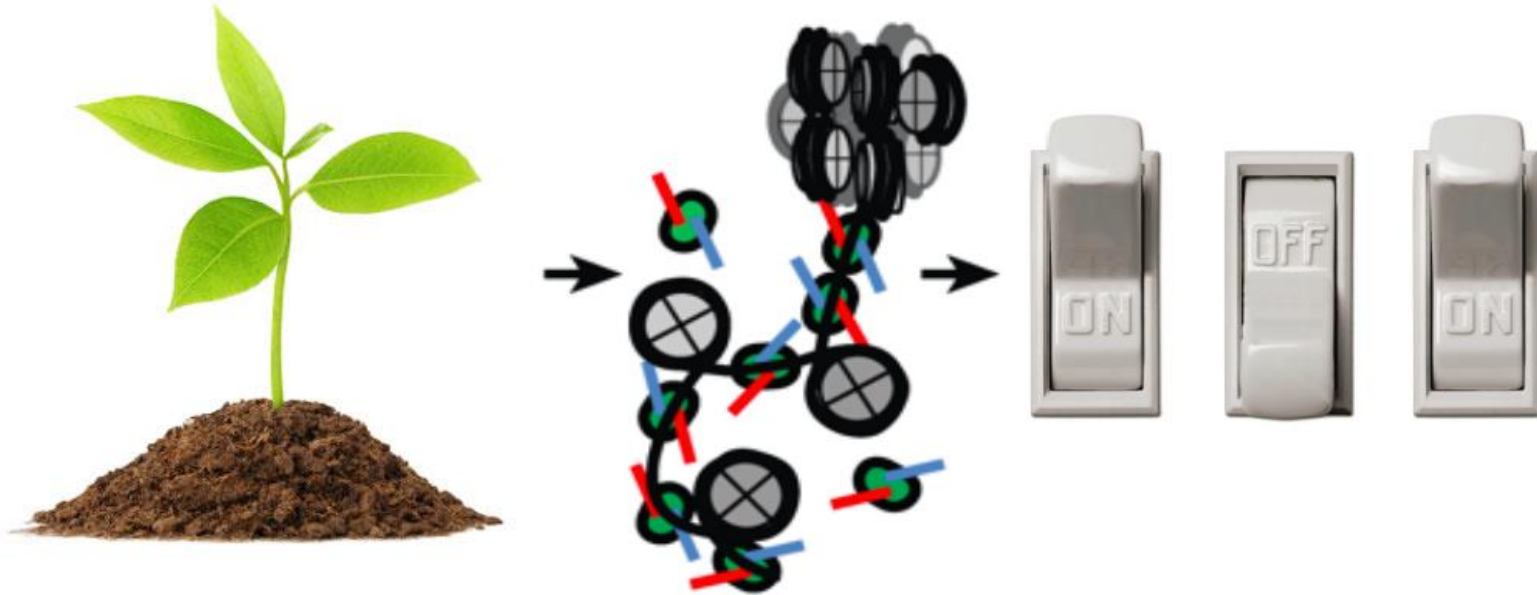
- Genome variants (1000 Genomes)
- Many regulators (ENCODE)
- Many many regulatory elements

## Navigation



- Fast: clinical time scale
- Sensitive: clinical samples
- Actionable: clinical decision criteria

# Measuring impact of environmental factors using plant epigenomics



- Continuously sample soil, air and water
- Material relative easy and inexpensive to obtain
- Able to sample from same plant over time
- Can perform follow-up experiments in controlled lab environment

# Acknowledgements



## Team

Fergus Chan - Co-founder  
Tracy Nance, PhD - Bioinformatics  
Marie Brennan, MD/PhD - Physician  
John Latham, PhD - Scientist  
Matt Negulescu, Software engineer  
Anupama Joshi, Software engineer

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Mike Snyder, PhD - Stanford  
Anshul Kundaje, PhD - Stanford  
Robert Tibshirani, PhD - Stanford  
Joseph Ecker, PhD - Salk

